REMARKS

The Office Action indicates that claims 1-12 are pending in the present application. However, the Applicants respectfully submit that Claims 14-20 were added by Preliminary Amendment on October 11, 2005. These claims were acknowledge in the restriction requirement mailed on May 31, 2007, which indicated the claims 1-20 were pending in the application. Therefore, the Applicants respectfully submit that claims 1-20 are pending in the present application. Claims 3-20 are withdrawn based on an election to a restriction requirement made on July 19, 2007 with a further election to SEQ ID NO:1. Thus, claims 1 and 2 were considered in the Office Action. Claims 1 and 2 stand rejected. No claim is objected to. Claims 1 and 2 are amended herein for clarity. Support for these amendments can be found, for instance, at page 3, line 24-29 as well as throughout the examples. Thus, no new matter is added.

Specification

The Specification is objected to for lacking sequence identifiers for the two sequences present on page 18, lines 29-32 of the specification as well as Figure 3. The Applicants amend page 18, lines 29-32 of the specification herein to include the sequence identifiers SEQ ID NOs: 27 and 28. They also provide a replacement sequence listing including these sequences.

Amendments to the Drawings

Figure 3 is objected to for not containing a sequence identifier. The Applicants herein submit a replacement figure in which the sequence identifier SEQ ID NO:16 is added to Figure 3. The Applicants respectfully submit that this sequence was included with the originally sequence listing. Thus, no new matter is added.

35 U.S.C. § 112, first paragraph

Claims 1-2 stand rejected under 35 U.S.C. §112, first paragraph as failing to comply with the enablement requirement. Specifically, the Examiner cites Tahlan, *et al. Antimicrobial Agents and Chemotherapy*, Mar. 2004; 48(3):930-939) as teaching that the

type of media is "important to both clavulanic acid and 5S clavam production." The Examiner alleges that there is additional experimentation that is necessary to make and use the microorganism with the recited limitation. Furthermore, the Examiner alleges that Tahlan, *et al.* teach that a high variation of clavulanic acid and 5S clavam production is observed by double mutants in SA and soy medium. The Examiner points out that there is a "nothing in the claims regarding differentiation of protein expression based on medium." With respect to the state of the art at the time the invention was made, the Examiner further alleges that the portion of the claims which is not enabled is the limitations reciting "wherein production of 5S clavams 'is reduced' and clavulanic acid production is 'at least maintained'." Based on Tahlan, *et al,* the Examiner alleges that no specific trend is observed when a single mutation of oat1 is made. Similarly, the Examiner alleges that double mutants of *S clavuligerus* are not enabled because Tahlan, *et al.* teach a "higher degree of variation in the level of 5S clavam metabolites" with no specific trend.

The Applicants respectfully submit that under the guidance provided by *In re Wands*, as cited by the Examiner, some experimentation may be necessary to practice a claimed invention. The test of enablement is not whether any experimentation is necessary, but whether it is undue. *In re Angstadt*, 537 F.2d 498, 504 (CCPA 1976). First, the Applicants respectfully submit that although Tahlan, *et al.* demonstrate that fermentation of different oat1 mutants may vary the amount of clavulanic acid produced in SA and soy medium, the range of production was about the same per medium. The variability appeared to be among mutants and not between media. Therefore, the Applicants respectfully submit that it is not necessary for the claims to recite a specific medium, because the Applicants demonstrate that certain mutants will effect clavulanic acid and/or 5S production. Tahlan, *et al.* merely shows that certain media can influence the amount of clavulanic acid and/or 5S clavams produced, but they do not suggest that, for instance, a mutant decreases clavulanic acid in one medium while the same mutant increases clavulanic acid production in a different medium. The trend is the same for each mutant; it is the degree of production that appears to be effected by the medium.

Similarly, Jensen, *et al.* show the effect of different types of media on the production of clavulanic acid and clavam metabolites in SA and soy medium. However, as shown in Table 2 of Jensen, *et al.* these metabolites are measured as a percentage of

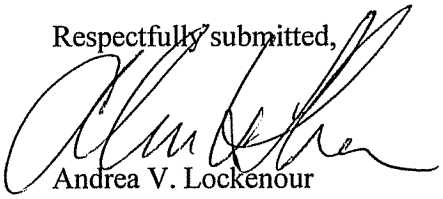
the same metabolite measure from wild type organism grown in soy medium. As is shown in Table 2, wild type produced considerably less clavulanic acid and metabolites when grown in SA medium compared with Soy. Thus, the medium can effect the production of clavulanic acid and clavam metabolites, but the trend appears to be the same for all mutants and wild type (i.e., a reduction of a production of these compounds in SA medium compared with Soy). More importantly, the mutation of certain genes can predicatively reduce the production of clavulanic acid and other clavams relative to wild type in both medium, regardless of media. It is merely the amount in the decrease in production compared with wild type that appears effected by media type.

Secondly, the applicants respectfully point out that the Examiner appears to assume that cvm6para of the present application is an alias for orf6 and OAT1 disclosed in Tahlan, *et al.* Table 1 of the current application identifies orf6paras having 47% identity with the ornithine acetyl transferase designated orf6 and OAT. cvm6para is an aminotransferase, with 66% identity with the acetlyornithine aminotransferase cvm6. Table 1 gives further designations for the genes in the paralogue cluster. The publication of Tahlan, *et al.* does not disclose cvm6par or cvm7par. A comparison of Figure 1 in the current application and figure 4 in Tahlan, *et al.* shows that Tahlan, *et al* discloses 4 genes designated ceaS1, bls1, pah1 and oat1. Table 1 in the present application identifies these genes as orf6par, orf4par, orf3par and orf2par, respectively. These genes correspond to the four genes on the right hand side of figure 1 and not to the three genes on the left hand side of figure 1, which include cvm6par and cvm7par. Thus, the cvm6para gene is not also known as orf6 and OAT1. The Applicants respectfully submit that the disclosure of Tahlan, *et al.*, therefore, cannot be used as a direct comparison with the current claims to determine their predictability and enablement.

The Applicants amend claims 1 and 2 for clarity herein to recite "the production of 5S clavams by said S. *clavuligerus* is reduced and clavulanic acid production is at least maintained when compared with a *S. clavuligerus* parent strain which has not had the relevant open reading frames disrupted or deleted." Support for these amendments can be found for example at page 3, line 24-29 as well as throughout the examples. The Applicants include these amendments for clarity and in no way acquiesce to the Examiner's rejections.

Applicants reserve the right to prosecute, in one or more patent applications, the claims to non-elected inventions, the cancelled claims, the claims as originally filed, and any other claims supported by the specification. Applicants thank the Examiner for the Office Action and believe this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration and allowance of the pending claims is earnestly solicited. If it would expedite the prosecution of this application, the Examiner is invited to confer with the Applicants' undersigned attorney.

Respectfully submitted,



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